Maina et al.

Serial No.: 10/586,720 Date Filed: July 20, 2006

Page 2

Amendments to the specification

Please amend the paragraph beginning on page 16, line 21, as follows:

"RNase III" refers to a naturally occurring enzyme or its recombinant form. The RNase III family of dsRNA-specific endonucleases is characterized by the presence of a highly conserved 9 amino acid stretch in their catalytic center known as the RNase III signature motif (see below). Mutants and derivatives are included in the definition. The utility of bacterial RNase III described herein to achieve silencing in mammalian cells further supports the use of RNases from eukarvotes, prokaryotes viruses or archea in the present embodiments based on the presence of common characteristic consensus sequences. Embodiments of the invention do not preclude the use of more than one RNase to prepare an RNA fragment mixture. Any RNase can be used herein where the RNase contains the amino acid consensus sequence [DEQ][\(\kappa \text{KRQT}\)[LM]E[FYW][LV]GD[SARH] (SEQ ID NO:27) (PROSITE: PDOC00448 documentation for the RNase III). While not wishing to be bound by theory, it is here suggested that there is a region in an RNAse III of this type that specifically contacts substrate RNA. This region includes 4 specific amino acids and it is here shown that a mutation in at least one particular amino acid of this region results in increased activity of the RNase III for purposes of producing dsRNA fragments. Figure 1 shows characteristic functionalities of RNases, Figure 2 shows conserved sequences in RNases from different sources. and Figure 12 shows a variety of mutations in different regions of the RNase III tested by applicants.